World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

PARATHYRIN IMPROVES GLUCOSE METABOLISM

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Article Received on 20/09/2019 **Article Revised on 10/10/2019** **Article Accepted on 30/10/2019**

ABSTRACT

The review contains contemporary and retrospective literature data about parathyrin effect and its interaction with calcium channel blockers concerning to glucose metabolism. It is shown that parathyrin decreases the blood glucose basal level, decreases the degree of hyperglycemia under glucose load, doesn't effect on insulin-stimulated glucose consumption by the muscle and adipose tissues *in vivo* and *in vitro*, increases glucose tolerance, i.e. parathyrin is gluco-regulating hormone. Calcium channels blockers (isoptin and nifedipin) led to much more decreasing of hyperglycemia under glucose-tolerance test against the background of parathyrin. It indicates the role of L-type Ca^{2+}-channel in the mechanisms of parathyrin effect on glucose homeostasis and testifies about parathyrin capacity to increase glucose tolerance.

KEYWORDS: Parathyrin, glucose metabolism, gluco-regulating hormone, insulin agonist, calcium channel blockers.

1. INTRODUCTION

Calcium-increasing hormone parathyrin (PTH) is the hormone of parathyroid glands, under which effect occurs the dynamic balance between bone calcium and blood serum. Homeostatic regulation of this balance provides with the influence of PTH on the resorptive processes in bone and as the result Ca^{2+} realizes. PTH increases calcium absorbtion in intestines and reabsorbtion in kidney small channels.

A number of investigations are showed that PTH activates Ca^{2+}entering in the cells of organs, not being its direct targets. PTH effect on glucose metabolism practically is unstudied. The single information about the increasing of PTH level in blood serum under diabetes mellitus.[1] and the metabolic syndrome.[2] is available.

Moreover, it is established the increasing of Ca and P excretion with urine under the metabolic syndrome, what positively correlated with the glycemia and the insulin level in blood.[2] and the intensification of bone resorption, that it is connected with the disturbance of Ca-P metabolism and the secretion of calcium-regulating hormones.[3] On the other hand, the disturbances of carbohydrate and lipid metabolism were revealed under the primary hyperparathyriosis.[4] There are some data about the stimulating effect of hypercalcaemia, induced by introducing of Ca-salts, which improved the assimilation of intra-vein glucose injection and increased the concentration of immunoreactive serum insulin.[5] It allowed suppose about the presence of PTH effect on the islet's apparatus of pancreas.

2. Parathyrin and Glucose Metabolism

It was showed the decreasing of the blood glucose level after one-time injection of parathyroidin (the preparation of bull PTH), which caused by hypercalcaemia, that confirms in tests with the calcium laktat load.[6] Besides, there is a close negative correlation established between glucose and calcium level (r =-0, 813, P>0,02). It is known that hypercalcaemia induces the increasing of insulin secretion.[7,8] Thereby, a special interest is the data about the decreasing of initial glucose level and the dynamics of alimentary hyperglycemia after PTH injection. Unlike other calcium-regulating hormone – calcium-decreasing hormone of the thyroid gland - calcitonin (CT), induced glucose intolerance,[9] PTH, on the contrary, decreasing the blood glucose level, decreased the degree of hyperglycemia under glucose load, i.e. it increased glucose tolerance.[6] Apparently, PTH due to hypercalcaemia stimulates insulin secretion, which, in one's turn, normalizes the blood glucose level and the same one doesn't make worse glucose tolerance. Analogues data were received under acute hypercalcaemia.[10] Besides it was established that PTH doesn't effect on insulin-stimulated glucose consumption by the muscle and adipose tissues *in vitro* and *in vivo.*[11]

3. Interaction of Parathyrin and Calcium Channel Blockers

Calcium channels blockers (isoptin and nifedipin) led to much more decreasing of hyperglycemia under glucose-tolerance test against the background of PTH.[6] It indicates the role of L-type Ca^{2+}-channel in the mechanisms of PTH effect on glucose homeostasis and testifies about PTH capacity to increase glucose tolerance. A special interest is the data of glucose consumption by muscle and adipose tissue *in vivo* and *in vitro*. Just like CT, PTH didn't effect on glucose consumption by these tissues but unlike CT.[11] it didn't change insulin-stimulating effect on this process.[6] Apparently, PTH, revealing its effect on non-specific receptors via Ca^{2+}-dependent processes, increases Ca^{2+} going out due to Ca^{2+}-channels L-type, that led to the decreasing of intracellular Ca^{2+} concentration in the muscle and adipose cells and furthers insulin-stimulating mobilization GLUT-4 from intracellular depot on plasmatic membranes, and this way, doesn't change insulin effect on glucose consumption by tissues, doesn't induce glucose intolerance and insulin resistance.

Thus, it is established the opposite to CT action of PTH on glucose metabolism. In this connection, it is acceptable to consider, that PTH is CT antagonist not only concerning to the regulation of calcium metabolism, but and glucose metabolism. So, it can take into consideration, that PTH takes part in neuro-endocrine regulation of carbohydrate metabolism being CT antagonist, i.e. PTH as CT.[12,13] is a gluco-regulating hormone.

4. Correlation of calcium and glucose metabolism

It is rather interesting to note that such glucose-increasing hormones as glucagon, ACTH, STH, glucocorticoids, thyroxin also occur and hypocalcaemic effect, i.e. as CT and PTH they take part in the regulation of calcium and glucose metabolism, that is an additional confirmation of the functional correlation of calcium and carbohydrate metabolism. The establishment of a functional negative correlation between glucose level and the total calcium content after PTH injections testifies about the close interconnection of calcium and glucose metabolism. With respect to interconnection of calcium-regulating hormones and its effect on glucose and calcium metabolism it can consider that under in vivo the effects of PTH can be, in the known degree, the result of changing of circulating $Ca^{2+,}$ in vitro indeed they must consider as the result of direct hormone effect. In other words, in the different cells not having a specialized receptors of PTH occur Ca^{2+}-dependent processes subordinated its regulating effects. Concerning to inter-correlation of the effects of calcium-regulating hormones on glucose metabolism one can suppose that, under hypercalcitoninemia and, correspondently, hypocalcaemia, PTH secretion intensifies, which, in one's turn, increases calcium level in blood serum, consequence of it there is the increasing of insulin secretion by pancreas β-cells. It is established, that hypercalcemia.[8] and the increasing of intercellular Ca^{2+} concentration take the important role in insulin secretion by pancreas β-cells.[7] CT, however, inhibits insulin secretion.[14,15] In addition, CT increases glucagon secretion, apparently, as it is mentioned above, due to the decreasing of the total calcium content in blood serum. Apparently, by this way a reciprocal interrelations between CT and PTH secretion and their effect on glucose and calcium metabolism occur, which reveals due to their modulating effect on insulin and glucagon secretion. Therefore, PTH acts as insulin agonist.

↑Parathormone secretion→Hypercalcemia→ ↑Insulin secretion→Hypoglycemia

Glucosa, calcium, β-cells function and calcium-regulating hormones are connected between them by feedback mechanisms.[16] Beyond all doubt, neuro-endocrine mechanisms of their interconnection require the further investigation. However, findings on this stage enlarge the conceptions about physiological role of PTH, testify about the involving of Ca^{2+}-mechanisms and give the basis to consider it as the important modulators of secret and metabolic processes.

REFERENCES

1. Mosin, VI, Iagoda, AV, Grossman, BE Blood levels of parathyroid hormone, calcitonin and cyclic adenosine monophosphate in diabetes mellitus. TerArkh, 1980; 52: 80-83.
2. Belych, OA, Geltser, BI, Kochetkova, EA Condition of Ca-P metabolism in young women with metabolic syndrome. Far-East Med J., 2006; 1: 54-58.
3. Belych, OA Functional metabolic mechanisms of remodelizing of bone tissue in young women with dishormonalpatholohy. Autoreferat diss. Doctor of Sciences (Medicine). Amursk State Medical Academy, 2006; 41.
4. Voronenko, IV, Mokrysheva, NG, Rozhinskaja, LYa Disturbances of carbohydrate and lipid metabolism under the primeryhyperthyriosis. Obesmetab, 2008; 4: 18-24.
5. Kakita, K, Kakita, S Analysis of immunoreactiveinsulins in man in relation to the effects of aging. Biochem Med, 1985; 34: 176-181.
6. Moisa, SS, Nozdrachev, AD One-time injection of parathyrin increases glucose tolerance. Open J EndocrMetabDis., 2013; 3: 293-300. DOI: 10.4236/ojemd.2013.38040.
7. Kim, HS, Yumkham, S, Lee HY, Cho JH, Kim MH, et al. C-terminal part of AgRP stimulates insulin secretion through calcium release in pancreatic beta Rin5mf cells. Neuropeptides, 2005; 39: 385-393.
8. Parthemore, JG, Deftos LJ Calcitonin secretion in normal human subjects. J ClinEndocrinolMetab, 1978; 47: 184-188.
9. Moisa, S.S. Contra-Insular Effect of Calcitonin on Glucose Metabolism. Bull Exp. Biol Med, 2013; 156: 217-219. DOI: 10.1007/s10517-013-2314-y.

10. Gedik, O, Akalin, S, Koray, Z Effect of acute hypercalcaemia on glucose tolerance and insulin release in human beings. ActaEndocrinol (Copenh), 1980; 94: 196-200.
11. Butakova (Moisa), SS, Nozdrachev, AD Effect of calcium-regulating hormones and calcium channel modulators on glucose consumption by muscle and adipose tissues in vivo and in vitro. Bull ExpBiol Med, 2009; 148: 171-174. https://doi.org/10.1007/s10517-009-0677-x.
12. Butakova (Moisa), SS, Nozdrachev AD Calcitonin – glucoregulating hormone. Vestnik Of Russian Military Medical Academy, 2010; 4: 188-196.
13. Moisa, SS, Nozdrachev, AD Mechanisms of calcium and carbohydrate metabolism regulation (Monograph) LAP LAMBERT Academic Publishing GmbH &Co., 2011; 319.
14. Iaroshevskii, YuA, Darinskii, YuA, Butakova (Moisa), SS Effect of calcitonin on insulin and glucagon secretion by the pancreas. ProblEndokrinol (Mosk), 1989; 35: 58-61.
15. Butakova (Moisa), SS Calcitonin, a modulater of pancreas secret process. Mechanisms of functioning of visceral systems: VI All-Russian Conf. with international participant devoted to the 50-th anniversary of discovery of membrane digestion by A.M. Ugolev. Thesis of addresses. Saint-Petersburg. Institute of Physiology named by I.P. Pavlov of The Russian Academy of Scienses, 2008; 26-27.
16. Zoloev, GK, Slepushkin, VD, Yakovleva, RA Relationships between the two-valency cationes, the function of the insular apparatus of pancreas and calcium-regulating hormones under the alteration of blood glucose level. Human Physiol, 1984; 10: 450-453.